REMARKS/ARGUMENTS

Rejection Under 35 USC 112, Second Paragraph

Claims 1-18 have been rejected under 35 USC 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. The word processing error referred to in the Office Action has been corrected by amendment.

In addition, the Patent Office objects to Applicant's choice of lettering steps (a) and (b) in method Claims 4 and 20. Claims 4 and 20 are dependent on Claims 1 and 19, respectively, which also recite steps (a) and (b) among others. This rejection has been obviated by amendment.

Rejection Under 35 USC 112, First Paragraph

Claims 25-27 and 31 have been rejected under 35 USC 112, first paragraph for lack of enablement. More specifically the Patent Office states that:

> ...the specification, while being enabling for detecting and quantifying clustered damages in DNA due to ionizing radiation, does not reasonably provide enablement for detecting and quantifying clustered damages due to a chemical agent such as a chemical carcinogen or a chemotherapeutic agent.

This rejection has been obviated by the Claim amendments set forth above. More specifically, Applicant has requested that Claims 25-27 and 31 be cancelled.

Rejections Under 35 USC 102

Claims 1-23 have been rejected under 35 USC 102(a) as being anticipated by Sutherland et al. (PNAS (2000) Vol. 97, No. 1, pages 103-108). In response to this rejection, Applicant has submitted a Declaration under 37 CFR 1.132 which makes clear that coauthors of the cited Sutherland et al. publication who were not named as inventors in the subject patent application did not contribute at the conceptual level to the invention as claimed. It is submitted that the entry of this Declaration obviates the stated grounds of this rejection.

Claims 1-8 are rejected under 35 USC 102(b) as being anticipated by Freeman et al (Analytical Biochemistry (1986) Vol. 158, pages 119-129: PTO-1449 reference AR2). More specifically the Patent Office states:

> Freeman et al. teach an agarose gel electrophoresis method for quantitating single strand breaks in nonirradiated DNA. In this method the number of average molecular lengths and length of average molecular lengths can be computed. Further, the frequency of the breaks can then be determined by comparison of the corresponding average molecular lengths of DNAs treated and not treated with inducing agents such as radiation, chemicals, or lesion-specific endonucleases...

Applicant respectfully traverses this rejection. Freeman et al. do not teach quantitatively determining the number average molecular length (L_n) of **double-stranded** DNA in the lesion-specific cleaving reagent-treated DNA and in the non-lesion-specific cleaving reagent treated-DNA. Rather, Freeman et al teach quantitatively determining the number average molecular length (L_n) of **single-stranded** DNA in the lesion-specific cleaving reagent-treated DNA and in the non-lesion-specific cleaving reagent treated-DNA. Freeman et al. teach denaturing DNA to be assayed prior to electrophoresis and as such does not anticipate Applicant's steps (c)-(e) of Claim 1. This distinction between Applicant's method and the method of Freeman et al is crucial for identifying clustered damages. Freeman et al. does not teach calculating the frequency of **clustered** damages in DNA to be assayed and therefore does not teach step (e) of Applicant's Claim 1. The method of Freeman et al. does not work for measuring clustered damages because the method is limited to determining the frequency of single-stranded breaks, or lesions convertible to single-strand breaks. Freeman et al. teaches denaturing the double-stranded DNA to be assayed prior to determining the number average molecular length of the resulting single-stranded DNA population. Because the strands are separated, information about the frequency of damages to one strand relative to another is lost. Freeman et al.

therefore is not enabling for calculating the frequency of **clustered** damages in DNA and thus does not anticipate Applicant's Claim 1.

Rejection Under 35 USC 103

Claims 1-24 and 28-30 are rejected under 35 USC 103(a) as being unpatentable over Freeman et al. (Analytical Biochemistry (1986) Vol. 158, pages 119-129: PTO-1449 reference AR2), in view of Wallace (Radiation Research (1998) Vol. 150 (Suppl. 5), pages S60-S79: PTO-1449 reference AT), in further view of Sutherland et al. (PNAS (2000) Vol. 97, No. 1, pages 103-108). More specifically, the Patent Office states:

> Freeman et al. teach an agarose gel electrophoresis method for quantitating single strand breaks in nonirradiated DNA...Wallace does teach Fgp protein, endonuclease III and endonuclease IV as lesion-specific enzymes...It would have been prima facie obvious...to utilize the enzymes of Wallace in the methods of Freeman et al...Sutherland et al. teach that their methods for investigations of biological organisms. It would have been prima facie obvious ...to use the methods of Freeman and Wallace to detect clustered DNA damage in an organism where the motivation is supplied by Sutherland.

Applicant respectfully traverses this rejection. Applicant submits for the reasons set forth above that Sutherland et al. is not available as a reference under 103(a)/102(a). Additionally, Applicant submits that the combination of Freeman et al. in view of Wallace does not teach calculating the frequency of clustered damages in DNA to be assayed and therefore does not teach all elements of Applicant's Claim 1. Simply put, substitution of the enzymes of Wallace in the methods of Freeman et al. **would not work** for calculating the frequency of **clustered** damages. Freeman et al. teaches denaturing the double-stranded DNA to be assayed prior to determining the number average molecular length of the DNA population. Because the strands are separated, information about the frequency of damages to one strand relative to another is lost. Modifying the method of Freeman et al. in view of Wallace would not enable one of ordinary skill in the art to calculate the frequency of **clustered** damages in DNA. Furthermore, Makrigiorgos et al. (Int. J. Radiation Biol. 74: 99-109 (1998)), a printed publication with a

reference date prior to Applicant's filing date yet subsequent to the publication date of Freeman et al., clearly states that gel electrophoresis-based methods to detect clustered damages in DNA, such as are used in model DNA studies, cannot be applied to genomic DNAs or mixtures of DNAs of unknown sizes. Makrigiorgos et al. characterizes the state of the art at the time the instant application was filed and clearly shows that it would not be obvious to one of ordinary skill in the art at the time the invention was filed to modify the method of Freeman in view of Wallace for calculating the frequency of **clustered** damages.

Summary

In light of the above amendment, consideration of the subject patent application is respectfully requested. Any deficiency or overpayment should be charged or credited to Deposit Account No. 02-3977.

Respectfully submitted,

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